

CLAIMS

1. A method for identifying an eRNA or a DNA sequence comprising an eRNA-encoding sequence in the nucleome of a eukaryotic cell, said method comprising identifying non-protein-encoding nucleotide sequences within an mRNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or between different cells' genomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same.

2. A method for identifying a receiver DNA or RNA sequence, said method comprising identifying non-protein-encoding nucleotide sequences within an RNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or between different cells' nucleomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same and then contacting said eRNA with nucleome and proteome material and screening for interaction between the eRNA and an DNA or RNA or protein wherein the detection of such an interaction is indicative of a receiver molecule.

3. The method of Claim 1 or 2 wherein the phenotyping comprises determining the degree to which a non-protein-encoding sequence is conserved within a cell's genome.

4. The method of Claim 1 or 2 or 3 wherein the phenotyping comprises determining the degree to which a non-protein-encoding sequence is conserved amongst genomes of different species, genera or families.
5. The method of Claim 1 or 2 wherein the phenotyping comprises determining a biological effect caused or associated with said non-protein-encoding sequence.
6. The method of Claim 1 or 2 wherein the eRNA is or is derived from an intron.
7. The method of Claim 1 or 2 wherein the eRNA is or is derived from an exon.
8. The method of Claim 2 wherein the receiver DNA or RNA is located in the coding sequence of a gene or its RNA transcript, in the 3' or 5' flanking region of a gene or its RNA transcript, in the intron or intron-exon junction of a gene or its RNA transcript, or in an intergenic (non transcribed) region of the genome.
9. The method of Claim 1 or 2 wherein the eukaryotic cell is from a vertebrate.
10. The method of Claim 1 or 2 wherein the eukaryotic cell is from an invertebrate.
11. The method of Claim 1 or 2 wherein the vertebrate is a mammal.
12. The method of Claim 1 or 2 wherein the vertebrate is an avian species.
13. The method of Claim 1 or 2 wherein the vertebrate is a reptilian species.

14. The method of Claim 1 or 2 wherein the vertebrate is an amphibian species.
15. The method of Claim 1 or 2 wherein the mammal is a human.
16. The method of Claim 1 or 2 wherein the eukaryotic cell is from a plant.
17. The method of Claim 1 or 2 wherein the plant is a monocotyledonous plant.
18. The method of Claim 1 or 2 wherein the plant is a dicotyledonous plant.
19. A method for identifying a receiver protein, said method comprising identifying non-protein-encoding nucleotide sequences within an RNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or between different cells' nucleomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same and then contacting said eRNA with proteome material and screening for interaction between the eRNA and a protein wherein the detection of such an interaction is indicative of a receiver protein.
20. The method of Claim 19 wherein the phenotyping comprises determining the degree to which a non-protein-encoding sequence is conserved within a cell's genome.
21. The method of Claim 19 wherein the phenotyping comprises determining the degree to which a non-protein-encoding sequence is conserved amongst genomes of different species, genera or families.

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22. The method of Claim 19 wherein the phenotyping comprises determining a biological effect caused or associated with said non-protein-encoding sequence.
23. The method of Claim 19 wherein the eRNA is an intron.
24. The method of Claim 19 wherein the eRNA is an exon.
25. The method of Claim 19 wherein the eukaryotic cell is from a vertebrate.
26. The method of Claim 19 wherein the eukaryotic cell is from an invertebrate.
27. The method of Claim 19 wherein the vertebrate is a mammal.
28. The method of Claim 19 wherein the vertebrate is an avian species.
29. The method of Claim 19 wherein the vertebrate is a reptilian species.
30. The method of Claim 19 wherein the vertebrate is an amphibian species.
31. The method of Claim 19 wherein the mammal is a human.
32. The method of Claim 19 wherein the eukaryotic cell is from a plant.
33. The method of Claim 19 wherein the plant is a monocotyledonous plant.
34. The method of Claim 19 wherein the plant is a dicotyledonous plant.
35. A method of modulating the phenotype of a cell, said method comprising identifying an eRNA associated with the particular phenotype by the method of Claim 1 or a receiver sequence for the eRNA by the method of Claim 2 or 19 and manipulating the cell to up-or down-regulate the level or activity of the eRNA or its receiver sequence to

thereby alter the phenotype of the cell.

36. The method of claim 35 wherein the eRNA is derived from an intron.

37. The method of claim 38 wherein the eRNA is derived from an exon.

38. The method of claim 38 wherein the receiver DNA is RNA is located in the coding sequence of a gene or its RNA transcript, in the 3' or 5' flanking region of a gene or its RNA transcript, in the intron or intron-exon junction of a gene or its RNA transcript, or in an intergenic (non transcribed) region of the genome.

39. The method of claim 35 wherein the eukaryotic cell is for a vertebrate.

40. The method of claim 35 wherein the eukaryotic cell is from an invertebrate.

41. The method of claim 35 wherein the vertebrate is a mammal.

42. The method of claim 35 wherein the vertebrate is an avian species.

43. The method of claim 35 wherein the vertebrate is a reptilian species.

44. The method of Claim 35 wherein the vertebrate is an amphibian species.

45. The method of Claim 35 wherein the mammal is a human.

46. The method of Claim 35 wherein the eukaryotic cell is from a plant.

47. The method of Claim 35 wherein the plant is a monocotyledonous plant.

48. The method of Claim 35 wherein the plant is a dicotyledonous plant.

49. A computer program product for assessing the likelihood of a candidate nucleotide sequence or group of nucleotide sequences being an eRNA or a receiver for an eRNA involved in network genetic signalling, said product comprising:-

- (1) code that receives as input index values for one or more of features wherein said features are selected from:
 - (a) the transmitter sequence is derived from an intron in a protein-coding RNA transcript or an intron or an exon in a non-protein-coding RNA transcript or their DNA equivalent;
 - (b) the target receiver sequence lies in an intron or an exon in an RNA transcript or its DNA equivalent;
 - (c) the target receiver sequence lies in an intergenic genomic DNA sequence, such as a promoter region;
 - (d) the target sequence is a DNA or RNA sequence capable of interaction with an eRNA;
 - (e) the target receiver sequence lies in a 5' untranslated region of an RNA transcript or its DNA equivalent;
 - (f) the target receiver sequence lies in a 3' untranslated region of an RNA transcript or its DNA equivalent;
 - (g) the target receiver is a protein capable of sequence-specific recognition of an eRNA and/or its target recognition sequences;
 - (h) the sequence is a DNA or RNA which recognizes and/or interacts with an eRNA;
 - (i) the sequence comprises at least 12 nucleotides;
 - (j) the sequence has at least 80% nucleotide identity or complementarity to at least one sequence of the same genome or nucleome; or

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- (k) the sequence has at least 80% nucleotide identity or complementarity to at least one sequence in a genome or nucleome of a different species, genus or family of animal or plant cells;
 - (l) The sequence associates its position to a feature from available databases, for example, Genbank, the Gene Ontology database or SWISSPORT; and
 - (m) The sequence associates by its position to a protein (ie. falls within the transcript) and that protein's expression profile, as determined by microarray analysis, is modulated in a specific way during a phenomena of interest, for example, highly up or down regulated in the initial phase of meiosis.
- (2) code that adds said index values to provide a sum corresponding to a predictive value for said candidate sequences; and
 - (3) a computer readable medium that stores the codes.

50. A computer program product for assessing the likelihood of a candidate nucleotide sequence or group of nucleotide sequences being a receiver molecule involved in network signalling *via* an eRNA, said product comprising:-

- (1) code that receives as input index values for one or more of features wherein said features are selected from:-
 - (a) the target receiver sequence lies in an intergenic genomic DNA sequence, such as a promoter region;
 - (b) the target receiver is a DNA or RNA sequence capable of interaction with an eRNA;

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- (c) the target receiver sequence lies in a 5' untranslated region of an RNA transcript or its DNA equivalent;
 - (d) the target receiver sequence lies in a 3' untranslated region of an RNA transcript or its DNA equivalent;
 - (e) the target receiver is a protein capable of sequence-specific recognition of an eRNA and/or its target recognition sequences;
 - (f) the sequence is a DNA or RNA which recognizes and/or interacts with an eRNA;
 - (g) the sequence comprises at least 12 nucleotides;
 - (h) the sequence has at least 80% nucleotide identity or complementarity to at least one sequence of the same genome or nucleome;
 - (i) the sequence has at least 80% nucleotide identity or complementarity to at least one sequence in a genome or nucleome of a different species, genus or family of animal or plant cells;
 - (j) The sequence associates its position to a feature from available databases, for example, Genbank, the Gene Ontology database or SWISSPORT; and
 - (k) The sequence associates by its position to a protein (ie. falls within the transcript) and that protein's expression profile, as determined by microarray analysis, is modulated in a specific way during a phenomona of interest, for example, highly up or down regulated in the initial phase of meiosis.
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- (2) code that adds said index values to provide a sum corresponding to a predictive value for said candidate sequences; and
 - (3) a computer readable medium that stores the codes.

51. A computer system for assessing the likelihood of a candidate sequence or group of candidate sequences being an eRNA involved in network genetic signalling wherein said computer system comprises:-

- (1) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise index values for one or more features, wherein said features are selected from:-
 - (a) the transmitter eRNA sequence is derived from an intron in a protein-coding RNA transcript or an intron or an exon in a non-protein-coding RNA transcript, or their DNA equivalent;
 - (b) the transmitter sequence comprises at least 12 nucleotides;
 - (c) the transmitter sequence has at least 80% nucleotide identity or complementarity to at least one sequence of the same genome or nucleome;
 - (d) the transmitter sequence has at least 80% nucleotide identity or complementarity to at least one sequence in a genome or nucleome of a different species, genus or family of animal or plant cells;
 - (e) the transmitter sequence comprises a secondary or tertiary structure having an activity; and
 - (f) the transmitter sequence exhibits catalytic activity;
- (2) a working memory for storing instructions for processing said machine-readable data;
- (3) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine readable data to provide a sum of said index values

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corresponding to a predictive value for said candidate sequences;
and

- (4) an output hardware coupled to said central processing unit for receiving said predictive value.

52. A computer system for assessing the likelihood of a candidate sequence or group of candidate sequences being a receiver RNA, DNA or protein involved in network genetic signalling wherein said computer system comprises:-

- (1) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise index values for one or more features, wherein said features are selected from:-
 - (a) the receiver sequence is located in an intron or an exon in an RNA transcript or its DNA equivalent;
 - (b) the receiver sequence lies in an intergenic genomic DNA sequence, such as a promoter region;
 - (c) the receiver sequence is located in a 5' untranslated region of an RNA transcript or its DNA equivalent;
 - (d) the receiver sequence is located in a 3' untranslated region of an RNA transcript or its DNA equivalent;
 - (e) the receiver sequence is a protein capable of sequence-specific recognition of an eRNA and/or its target recognition sequence;
 - (f) the receiver sequence is an RNA or DNA which recognizes and/or interacts with an eRNA;
 - (g) the receiver sequence comprises at least 12 nucleotides;

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- (h) the receiver sequence has at least 80% nucleotide identity or complementarity to at least one sequence of the same genome or nucleome;
 - (i) the receiver sequence has at least 80% nucleotide identity or complementarity to at least one sequence in a genome or nucleome of a different species, genus or family of animal or plant cells;
 - (j) the receiver sequence comprises a secondary or tertiary structure having an activity; and
 - (k) the receiver sequence exhibits catalytic activity;
- (2) a working memory for storing instructions for processing said machine-readable data;
 - (3) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine readable data to provide a sum of said index values corresponding to a predictive value for said candidate sequences; and
 - (4) an output hardware coupled to said central processing unit for receiving said predictive value.

53. An eRNA molecule identified by the method comprising identifying non-protein-encoding nucleotide sequences within an RNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or

between different cells' nucleomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same.

54. A receiver DNA or RNA identified by the method comprising identifying non-protein-encoding nucleotide sequences within an RNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or between different cells' nucleomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same and then contacting said eRNA with nucleome material and screening for interaction between the eRNA and a DNA, RNA or protein wherein the detection of such interaction is indicative of a receiver molecule.

55. A receiver protein identified by the method comprising identifying non-protein-encoding nucleotide sequences within an RNA transcript or a DNA sequence encoding same in said nucleome, determining the nucleotide sequence of said non-protein-encoding nucleotide sequence and subjecting said sequence to phenotyping to determine its effect on one or more biological events within a cell and/or determining the degree to which said sequence is conserved in the cell's genome or in the genome of other species or genera of eukaryotic cells wherein a non-protein-encoding nucleotide sequence having a biological effect in a cell or a nucleotide sequence conserved within the genome or between different cells' nucleomes is deemed to be an eRNA or DNA sequence comprising a nucleotide sequence encoding same and then contacting said eRNA with proteome material and screening for interaction between the eRNA and a protein wherein the detection of such interaction is indicative of a receiver protein.

56. A method of inducing post transcriptional gene silencing (PTGS) in a eukaryotic cell, said method comprising identifying an eRNA having a receiver sequence

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in a target gene to be silenced and expressing a DNA comprising said eRNA in said cell for a time and under conditions sufficient for the target gene to be silenced.

57. The method of claim 56 wherein the cell is a plant cell.

58. The method of claim 56 wherein the cell is a mammalian cell.

59. The method of claim 58 wherein the mammalian cell is a human cell.

60. Use of an eRNA or an analog or homolog to modify a genetic network in a cell to thereby alter a cell's phenotype.

61. A method for detecting an altered genetic network said method comprising screening for the presence or absence of an eRNA or an altered level of eRNA wherein an alteration in the presence, absence or level of eRNA is indicative of an altered genetic network and thereby an altered phenotype.